CLAIMS

We Claim:

1. A molecule of the structure **A – X – B**, wherein

B is a peptide portion of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake,

A is a peptide portion of about 2 to about 20 acidic amino acid residues, which when linked with portion **B** is effective to inhibit or prevent cellular uptake of portion **B**, and

X is a linker of about 2 to about 100 atoms joining **A** with **B**, which can be cleaved under physiological conditions.

2. The molecule of claim 1, wherein said peptide portion **A** comprises about 5 to about 9 glutamates or aspartates.

3. The molecule of claim 2, wherein said peptide portion **A** comprises about 5 to about 9 consecutive glutamates or aspartates.

4. The molecule of claim 1, wherein said peptide portion **B** comprises about 9 to about 16 arginines.

5. The molecule of claim 4, wherein said peptide portion **B** comprises about 9 to about 16 consecutive arginines.

6. The molecule of claim 1, wherein said peptide portion **A** comprises D-amino acids.

7. The molecule of claim 1, wherein said peptide portion **B** comprises D-amino acids.

8. The molecule of claim 1, wherein said peptide portion **A** consists of D-amino acids.

9. The molecule of claim 1, wherein said peptide portion **B** consists of D-amino acids.

10. The molecule of claim 1, wherein said peptide portions **A** and **B** consists of D-amino acids.

11. A molecule for transporting a cargo moiety across a cell membrane of the structure **A – X – B - C**, wherein

C is a portion comprising a cargo moiety,

B is a peptide portion of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, is covalently linked to portion **C**, and is effective to enhance transport of cargo portion **C** across a cell membrane,

A is a peptide portion of about 2 to about 20 acidic amino acid residues, which when linked with portion **B** is effective to inhibit or prevent cellular uptake of **B - C** , and

X is a cleavable linker of about 2 to about 100 atoms joining **A** with **B – C,** which can be cleaved under physiological conditions.

12. The molecule of claim 11, wherein said peptide portion **A** comprises amino acids selected from the group of acidic amino acids consisting of glutamate and aspartate.

13. The molecule of claim 11, wherein said peptide portion **B** comprises amino acids selected from the group of basic amino acids consisting of arginine and histidine.

14. The molecule of claim 11, wherein said cargo portion **C** is selected from the group of cargo moieties consisting of a fluorescent moiety, a fluorescence-quenching moiety, a radioactive moiety, a radiopaque moiety, a paramagnetic moiety, a nanoparticle, a vesicle, a molecular beacon, a marker, a marker enzyme, a contrast agent, a chemotherapeutic agent, and a radiation-sensitizer.

15. The molecule of claim 14, wherein the cargo portion **C** comprises a contrast agent for diagnostic imaging.

16. The molecule of claim 14, wherein the cargo portion **C** comprises a radiation sensitizer for radiation therapy.

17. The molecule of claim 11, wherein said peptide portion **A** comprises about 5 to about 9 glutamates or aspartates.

18. The molecule of claim 17, wherein said peptide portion **A** comprises about 5 to about 9 consecutive glutamates or aspartates.

19. The molecule of claim 11, wherein said portion peptide **B** comprises between about 9 to about 16 arginines.

20. The molecule of claim 19, wherein said peptide portion **B** comprises between about 9 to about 16 consecutive arginines.

21. The molecule of claim 11, wherein said peptide portion **A** comprises D-amino acids.

22. The molecule of claim 11, wherein said peptide portion **B** comprises D-amino acids.

23. The molecule of claim 11, wherein said peptide portion **A** consists of D-amino acids.

24. The molecule of claim 11, wherein said peptide portion **B** consists of D-amino acids.

25. The molecule of claim 11, wherein said peptide portions **A** and **B** consist of D-amino acids.

26. The molecule of claim 25, wherein said peptide portion **B** consists of D-arginine amino acids.

27. The molecule of claim 11, wherein said peptide portion **A** is located at a terminus of a polypeptide chain comprising **B - C**.

28. The molecule of claim 11, wherein said peptide portion **A** is located at the amino terminus of a polypeptide chain comprising **B - C**.

29. The molecule of claim 11, wherein said peptide portion **A** is linked near to or at the amino terminus of a polypeptide chain comprising **B - C**.

30. The molecule of claim 11, wherein said peptide portion **A** is linked near to or at the carboxy terminus of a polypeptide chain comprising **B - C**.

31. The molecule of claim 11, wherein **B – C** comprises a polypeptide chain having ends consisting of a **B-side** terminus and a **C-side** terminus, and wherein cleavable linker **X** is disposed near or at said **B-side** terminus.

32. The molecule of claim 11, wherein **B – C** comprises a polypeptide chain having ends consisting of a **B-side** terminus and a **C-side** terminus, and wherein cleavable linker **X** is disposed near or at said **C-side** terminus.

33. The molecule of claim 11, wherein cleavable linker **X** is a flexible linker.

34. The molecule of claim 11, wherein cleavable linker **X** is a flexible linker about 6 to about 30 atoms in length.

35. The molecule of claim 11, wherein cleavable linker **X** is cleavable in an acidic environment.

36. The molecule of claim 11, wherein cleavable linker **X** is comprises a peptide linkage.

37. The molecule of claim 11, wherein cleavable linker **X** comprises aminocaproic acid.

38. The molecule of claim 11, wherein cleavable linker **X** is configured for cleavage exterior to a cell.

39. The molecule of claim 11, wherein cleavable linker **X** is configured for cleavage by an enzyme.

40. The molecule of claim 38, wherein said enzyme is a matrix metalloprotease.

41. The molecule of claim 35 wherein cleavable linker **X** comprises the amino acid sequence PLGLAG (SEQ ID NO:1).

42. The molecule of claim 35 wherein cleavable linker **X** comprises the amino acid sequence EDDDDKA (SEQ ID NO:2).

43. The molecule of claim 34 wherein cleavable linker **X** comprises a **S - S** linkage.

44. The molecule of claim 34, wherein cleavable linker **X** comprises a transition metal complex, wherein said transition metal complex linker is cleaved when the metal is reduced.

45. The molecule of claim 11, comprising a plurality of cleavable linkers **X** linking a portion **A** to a structure **B - C.**

46. A pharmaceutical composition comprising:

A molecule of the structure **A – X – B**, wherein

B is a peptide portion of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake,

A is a peptide portion of about 2 to about 20 acidic amino acid residues, which when linked with portion **B** is effective to inhibit or prevent cellular uptake of portion **B**, and

X is a cleavable linker of about 3 to about 30 atoms joining **A** with **B**, which can be cleaved under physiological conditions; and

a pharmaceutically acceptable carrier.

47. The pharmaceutical composition of claim 46, wherein

said cleavable linker **X** is of between about 6 to about 30 atoms in length, said portion **A** has between about 5 to about 9 acidic amino acid residues, and said portion **B** has between about 9 to about 16 basic amino acid residues.

48. The pharmaceutical composition of claim 46 or 47, further comprising a portion **C** covalently attached to said portion **B** and comprising a cargo moiety.

49. A method of modulating cellular uptake of a peptide **B** of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, comprising:

linking said peptide **B** to a peptide **A** of about 2 to about 20 acidic amino acid residues with a cleavable linker **X** of about 3 to about 30 atoms, which can be cleaved under physiological conditions and

cleaving said cleavable linker **X** effective to separate peptide **B** from molecule **A**.

50. A method of modulating cellular uptake of a cargo moiety **C**, comprising:

covalently attaching a cargo moiety **C** to a peptide **B** of about 5 to about 20 basic amino acid residues to form a molecule **B - C**;

linking said molecule **B - C** to a peptide **A** of about 2 to about 20 acidic amino acid residues with a cleavable linker **X** of about 3 to about 30 atoms, and

cleaving said cleavable linker **X** effective to separate **B - C** from said peptide **A**.

51. A nucleic acid encoding a molecule of the structure **A – X – B**, wherein

B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake,

A is a peptide of about 2 to about 20 acidic amino acid residues, which when linked with peptide **B** is effective to inhibit or prevent cellular uptake of peptide **B**, and

X is a cleavable linker portion of between 1 and 10 amino acid residues joining **A** with **B**, which can be cleaved under physiological conditions.

52. A nucleic acid encoding a molecule of the structure **A – X – B – C**, wherein

C is a peptide cargo moiety,

B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake,

A is a peptide of about 2 to about 20 acidic amino acid residues, which when linked with peptide **B** is effective to inhibit or prevent cellular uptake of peptide **B - C**, and

X is a cleavable linker portion of between 1 and 10 amino acid residues joining **A** with **B – C** which can be cleaved under physiological conditions.

53. A molecule for transporting a fluorescent cargo moiety across a cell membrane of the structure **Q - A – X – B - C**, wherein

C is a portion comprising a fluorescent cargo moiety,

B is a peptide portion of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, is covalently linked to portion **C**, and is effective to enhance transport of cargo portion **C** across a cell membrane,

Q is a quencher moiety attached to A and effective to quench fluorescence from fluorescent cargo **C**;

A is a peptide portion of about 2 to about 20 acidic amino acid residues, which when linked with portion **B** is effective to inhibit or prevent cellular uptake of **B - C** , and

X is a cleavable linker of about 2 to about 100 atoms joining **A** with **B – C**, which can be cleaved under physiological conditions.

54. The molecule of claim 39, wherein said enzyme is a protease.

55. The molecule of claim 54, wherein, upon cleavage of said linker **X**, said linker **X** has a C-terminus and said portion **B** has an **N** terminus, whereby upon cleavage of linker **X** said N terminus of portion **B** may provide an additional positive charge to portion **B** under physiological conditions.

56. The molecule of claim 11, comprising a single cargo portion **C** linked to a plurality of portions **B**, each of portions **B** being linked to a cleavable linker portion **X** linked to an acidic portion **A.**